



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,894	07/17/2003	Georg Watzek	35931-PCT-USA-A 071986.02	1493
21003	7590	02/12/2008	EXAMINER	
BAKER BOTTS L.L.P. 30 ROCKEFELLER PLAZA 44TH FLOOR NEW YORK, NY 10112-4498			AFREMOVA, VERA	
			ART UNIT	PAPER NUMBER
			1657	
			NOTIFICATION DATE	DELIVERY MODE
			02/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DLNYDOCKET@BAKERBOTTS.COM

Office Action Summary	Application No. 10/621,894	Applicant(s) WATZEK ET AL.	
	Examiner Vera Afremova	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Claims 17-26 as amended (10/31/2007) are pending and under examination in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-21 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,165,938 (Kington).

Claims are directed to a drug composition for topical application as intended for wound healing wherein the composition comprises microparticles from activated thrombocytes and extracellular matrix material. The microparticles are prepared by activating thrombocytes with an activating agent selected from collagen, thrombin, calcium ionophore A23187 or C5b-9 in a liquid medium and by separating the microparticles from the liquid medium by centrifugation, filtration or chromatography. Some claimed are further drawn to the virus inactivation and/or

depletion in the drug product-obtained-by-process. Some claims are further drawn to the presence of matrix materials, collagen, fibrinogen, thrombin and/or organic polymers and inorganic compounds in the drug composition. Some claims are further drawn to incorporation of biocompatible materials into the drug composition or to a metal surface treated with the drug composition.

US 5,165,938 (Kington) discloses a drug composition produced from blood and intended for topical application and wound healing (abstract). The drug composition contains “microparticles” derived from platelet-rich plasma after activation with collagen and centrifugation. The “microparticles” are mixed with microcrystalline collagens and frozen (col. 2, lines 20-55 or col.3, lines 25-44). The drug composition is made under sterile condition (col.3, line 26). Blood is collected from normal patients that are not diagnosed with viral diseases and, thus, virus depleted or virus free. The cited patent discloses that drug composition contains growth factors PDAF and PDGF or substances promoting wound healing. Fibrinogen and thrombin are inherent components of a product derived from platelet rich plasma. Proteins and/or glycoproteins of platelet rich plasma fall within the meaning of generic organic polymers as claimed. The drug composition contains inorganic compounds or inorganic salts (col. 3, line 42). The cited patent teaches the use of composition in conjunction with either biodegradable dressings or with some implantable devices (col. 4, lines 32-35).

Thus, the cited patent anticipates the claimed invention.

Claims 17-21 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,185,160 (Chao) in the light of evidence by Exner et al. (Blood Coagulation and Fibrinolysis. 2003, 14:773-779).

Claims as above.

US 5,185,160 (Chao) discloses a pharmaceutical composition suitable to treat wounds (col. 3, line 34) and comprising viral-inactivated blood platelet membrane microparticle fractions (abstract). The microparticle fractions are made by activation of platelets by repeated freezing thawing and the microparticle fractions are separated or collected by centrifugation (col. 4, lines 1-60). Exner et al. evidence the inherent fact that freezing-thawing activates platelets, for example: see abstract. The product of the cited US 5,185,160 is subjected to virus inactivation by heat treatment (abstract and col. 4, lines 40-45). Proteins and/or glycoproteins (GPIb, for example: col. 5, line 11) in the final preparation of US 5,185,160 as disclosed fall within the meaning of generic extracellular matrix materials and/or biocompatible materials. The cited preparation with microparticles is suitable for wound healing (col. 3, line 34).

Thus, the cited patent US 5,185,160 (Chao) anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,165,938 (Kington), US 5,185,160 (Chao), US 5,552,290 (Michelson et al) and US 5,697,980 (Otani et al.).

Claims are directed to a drug composition for topical application as intended for wound healing wherein the composition comprises microparticles from activated thrombocytes and extracellular matrix material. The microparticles are prepared by activating thrombocytes with an activating agent selected from collagen, thrombin, calcium ionophore A23187 or C5b-9 in a liquid medium and by separating the microparticles from the liquid medium by centrifugation, filtration or chromatography. Some claimed are further drawn to the virus inactivation and/or depletion in the drug product-obtained-by-process. Some claims are further drawn to the presence of matrix materials, collagen, fibrinogen, thrombin and/or organic polymers and inorganic compounds in the drug composition. Some claims are further drawn to incorporation of biocompatible materials into the drug composition including titanium and apatite. Some claims are further drawn to a metal surface treated with the drug composition.

US 5,165,938 (Kington) and US 5,185,160 (Chao) are relied upon as explained above for the disclosure of drug compositions intended for wound healing and comprising microparticles derived from the activated platelets and extracellular matrix carriers. The microparticles are derived from the activated platelets, separated by centrifugation and incorporated into the drug compositions disclosed by US 5,165,938 (Kington) and US 5,185,160 (Chao). The cited products are made under sterile conditions, thereby, being free of contaminants or viral infection. In particular, US 5,185,160 (Chao) teaches the drug composition is subjected to viral inactivation.

US 5,165,938 (Kington) teaches that the microparticles are made by activating platelets with an activating agent such as collagen. In addition, the cited US 5,552,290 is relied upon for the teaching that the platelet-derived microparticles are made by activation of platelets with various activating agents including collagen, thrombin, ionophore A23187 and protein C5b-9 (col. 1, lines 43-45 and col.3, lines 4-13).

US 5,165,938 (Kington) teaches incorporation of microparticles derived from the activated platelets into wound dressing materials and into coating materials over the devices utilized in surgical procedures that would include at least some surgical metal devices and/or instruments.

But the cited patents are missing particular disclosure about the use of titanium, apatite and organic polymers as materials for carriers and/or medical devices. However, US 5,697,980 (Otani et al.) teaches artificial filling and prosthetic device(s) capable of adhering to tissues or to wounded tissues wherein the materials include titanium core coated with calcium phosphate (apatite) and organic polymers including polycaprolactone or polyactone. For example: see abstract; col. 2, line 26 and lines 37-40; col. 3, lines 33-45 and col. 4, lines 10-17).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add various carriers, fillings, biodegradable materials and devices including titanium, apatite and organic polymers to modify the drug compositions taught by US 5,165,938 (Kington) and/or US 5,185,160 (Chao) as suggested by US 5,165,938 (Kington) with a reasonable expectation of success in wound healing because the claimed carriers and materials are known and used for making artificial filling, carriers and medical devices as adequately demonstrated by US 5,697,980 (Otani et al.). One of skill in the art would

have been motivated to adjust carrier compositions of US 5,165,938 (Kington) and of US 5,185,160 (Chao) with regard to a mode of administration for the expected benefits in wound healing and/or in bleeding reduction as provided by microparticles derived from blood platelets. The knowledge about the use of various platelet activating agents for making and collecting the platelet derived microparticles is available in the prior art as adequately demonstrated by US 5,552,290 (Michelson et al).

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicants' arguments filed 10/31/2007 have been fully considered but they are not persuasive.

With respect to the claims rejected under 35 U.S.C. 102(b) as being anticipated by US 5,165,938 (Kington) applicants appear to argue that the claimed invention is directed to microparticles separated "from" supernatant (thrombocyte supernatant) unlike the cited product that is present "in" supernatant (response page 5-7). This argument neither has persuasive grounds nor it is true. First, the claimed invention does not recite what is discarded and what is retained. Further, the cited reference clearly teaches that the activated platelet rich plasma is subjected to a removal of platelets and fibrin by centrifugation and that the resulting supernatant is a source of molecules or "microparticles" such as PDGF and PDAF that are released from the

activated platelets (col. 2, lines 31-40 and col. 3, lines 59-67). The cited patent clearly teaches molecular weight of “microparticles” such as PDGF and PDAF and, thus, they are separated “from” supernatant as argued. The cited final product such as the PDGF and PDAF-containing supernatant has the wound healing effects as the claimed product. Thus, the final product is the same the claimed product-obtained-by-process within the meaning of the claims. Neither specification nor claims define the structure of “microparticles” released from the activated platelets in order to distinguish between materials separated during centrifugation after activation of platelets as argued.

With regard to the claim rejected under 35 U.S.C. 102(b) as being anticipated by US 5,185,160 (Chao) applicants argue that the Chao’s patent refers to “microparticles” that are not the same as the “microparticles” of the present invention because 1) the starting platelets utilized in the Chao’s method are not necessarily activated and 2) there is no basis to assume that activation with freeze-thawing is the same as the presently claimed (response page 8).

These arguments are not found persuasive because the product-by-process claims are not limited to the manipulations of the recited steps, only the final structure implied by the steps. MPEP 2113. The final structure or nature of the claimed “microparticles” is no more than some generic compounds derived from activated platelets as claimed and they could be any and all cell components as disclosed (specification page 5, line 1). The Chao’s “microparticles” are platelet membrane microvesicles (see title) that are obtained by repeated freezing-thawing cycles. The inherent fact that platelets are activated by freezing-thawing is evidenced by Exner et al., for example: see abstract. Accordingly to the Horstman’s definitions (IDS reference) microparticles

are membrane vesicles or membrane fractions released by platelets during activation and they have procoagulant activity and PF3 activity (see page 113, col.1, par. 1 and par. 3). The Chao's patent teaches exactly the same preparation of platelet-derived microparticles as defined by Horstman (IDS reference) that are platelet membrane microparticle fractions (col. 2, lines 26-27), that have procoagulant activity (col. 2, line 38) and they have PF3 activity (col. 3, line 18). Thus, the microparticles of Chao have the same structure or the same "moieties" as the applicants' claimed microparticles and they have the same activity as the applicants' microparticles as argued, as defined in the as-field specification and in the light of the prior art definitions.

The evidentiary reference by Lindeman has been reviewed. Applicants appear to argue that as evidenced by Lindeman the freeze-thawing submetabolic temperatures of the Exner' protocol and/or of the Chao's protocol would not favor synthesis of inflammatory mediators. However, the reference by Lindeman is silent about activation by freeze-thawing. Further, it is unclear whether and/or what "inflammatory mediators" are intended for the applicants' invention. Furthermore, the reference by Lindemann teaches that, for example: IL-1 beta protein is induced by platelet activation and also shed by mature membrane microvesicles (abstract). Thus, even if the Chao's microparticles might not be separated from supernatant of the activated platelets, the Chao's microparticles would still provide for at least some amounts of IL-1 beta protein.

The evidentiary reference by Alberio has been reviewed. Applicants appear to argue that as evidenced by Alberio different agents are associated with different activated platelets phenotypes. Yet, neither phenotype of activated platelet nor final nature of "microparticles"

obtained from the activated platelet is recited and/or encompassed for applicants' product as claimed and as disclosed. Moreover, reference by Alberio appears to demonstrate that various collagen types activate platelets of the same phenotype to more or less different extend (fig. 4) and that effect of the same agent is dose-dependent (fig. 3).

Thus, there is no reason to believe that the "microparticles" of US 5,185,160 (Chao) might be different from the claimed "microparticles".

With regard to claim rejection under 35 USC § 103 applicants argue that there is no suggestion, motivation and/or reasonable expectation in success for the combination of cited references because platelet activation elicits a variety of physiological responses as supported by evidentiary reference by Gemmeli et al. (response pages 9-10). However, final nature of "microparticles" obtained from the activated platelet is not recited for the applicants' product as claimed and as disclosed. The references cited in the office action are in the same field of endeavor such as drug compositions intended for wound healing and comprising the platelet-derived microparticles and they seek to solve the same problems as the instant application and claims such as provide for the wound healing and comprising the platelet-derived microparticles, and one of skill in the art is free to select components available in the prior art, *In re Winslow*, 151 USPQ 48 (CCPA, 1966).

No claims are allowed.

Application/Control Number:
10/621,894
Art Unit: 1657

Page 11

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova,

AU 1657

February 5, 2008



VERA AFREMOVA

PRIMARY EXAMINER